REMARKS

This application is amended in a manner believed to place it in condition for allowance at the time of the next Official Action.

A new Declaration under Rule 132 is included in this amendment. The declaration filed July 13, 2007, which demonstrated the synergistic effect of the claimed included a typographical error, i.e., Boswellia extract "senolee". This new declaration accurately reflects the Boswellia extract that was evaluated, i.e., Boswellia extract "serrata".

Status of the Claims

Claims 1 and 2 are amended to define the "derivatives" in a manner consistent with the originally filed specification, for example, at page 2, lines 3-10 and 22.

Claims 1-5, 7 and 8 are all amended to form and remain pending in the application.

Claim Rejections-35 USC §112

Claims 1-5, 7 and 8 were rejected under 35 U.S.C. §112, second paragraph, for being indefinite. This rejection is respectfully traversed for the reasons below.

One position of the Official Action was that the specification did not give a list saligenin, boswellic acid and lipophilic derivatives.

However, as described at page 2, line 3, "Examples of saligenin derivatives comprise the acetic or butyric esters, whereas examples of boswellic acid derivatives comprise pharmaceutically acceptable salts or esters." Accordingly, these derivatives are now recited in a manner consistent with the specification.

As to the lipophilic derivatives the procyanidins may be optionally complexed with "phospholipids or rhein" as disclosed on line 10 of specification page 2. It is noted that such phospholipids complexes are further exemplified by incorporation by reference of US 4.963,527 on line 22 of page 2.

Another position of the Official Action was that the phrase "boswellic acid-enriched Boswellia serrata extract" was unclear. This is "enriched" extract, i.e., the extract has a particularly high content of boswellic acid concentration.

Therefore, the claims are definite and withdrawal of the rejection is respectfully requested.

Claim Rejections-35 USC §103(a)

Claims 1-4 were rejected under 35 USC §103(a) as being unpatentable over FOSTER, TANEJA et al. U.S. 5,629,351 (TANEJA), RONZIO et al. U.S. 5,762,936 ("RONZIO"), CHARTERS et al. U.S. 6,541,045 ("CHARTERS"), SATO et al. 1967 ("SATO"). This rejection is respectfully traversed for the reasons that follow.

FOSTER was offered for teaching treating rheumatism and inflammation using saligenin. The Official Action acknowledged that FOSTER fails to disclose or suggest any of the other active principles as claimed.

TANEJA was offered for teaching that the gum resin of Boswellia serrata has been used for the treatment of arthritis at 10g in a range from 1-55% by weight of a composition.

RONZIO was offered for teaching a phenolics content from about 1-6 mg of catechins, which contain procyanidin, for treating inflammation. The Official Action noted that procyanidin may be isolated from green tea leaves. The Official Action apparently intended to propose that one of ordinary skill would have been motivated to isolate procyanidin from green tea leaves.

CHARTERS was offered for teaching an anti-inflammatory drug having N-acetyl D-glucosamine.

SATO was offered for teaching anti-inflammatory activity of D-glucuronolactone.

The position of the Official Action is that it would have been obvious to combine the ingredients above-listed ingredients because these ingredients were disclosed for treating inflammation.

However, the claims are unobvious over the combination for at least the following five reasons:

I. CHARTERS fails to teach that for which it was offered.

CHARTERS discloses herbal compositions against inflammation. However, for *the purpose of inflammation*, i.e., the motivation cited in the Official Action for combining the documents, CHARTERS fails to disclose or suggest that N-acetyl glucosamine is effective.

Instead, CHARTERS discloses therapeutically effective amounts of Japanese knotweed, Devil's claw, grapeskin and syzygium for the purpose of treating inflammation (See, e.g., the abstract).

CHARTERS discloses N-acetyl glucosamine as merely one of about 16 "therapeutically effective" ingredients, i.e., as noted in column 5, lines 38-44. Indeed, the abstract notes that N-acetyl glucosamine is therapeutically effective for soothing muscles and joints, which CHARTERS recognizes as separate from treating inflammation. Indeed, CHARTERS explains the activity of N-acetyl glucosamine as being a rate-limiting factor in hyaluronic acid production by living cells. See, e.g., column 8, lines 1-19.

Thus, CHARTERS fails to teach n-acetyl d-glucosamine for the purpose of treating inflammation, and there would have been no reason to combine n-acetyl d-glucosamine with FOSTER or other documents for the purpose of treating inflammation.

II. RONZIO fails to teach that for which it was offered.

RONZIO discloses a lentil husk extract for treating inflammation, and the extract contains a phenolics mixture that includes 1 to 6 mg of catechin equivalents per 10 milligrams of the extract. This phenolics mixture comprises kaempferol, quercetin, proanthocyanidins and phenolic acids. Of the proanthocyanidins, at least 50%, and preferably at least 70% are in the form of prodelphinidin, while the proanthocyanidins merely "include" procyanidin. Thus, prodelphinidin appears to be more preferred. See, e.g., the abstract, column 5, lines 25-65.

Accordingly, contrary to the apparent position held by the Official Action, one of ordinary skill in the art would not have been persuaded to derive procyanidin from green tea leaves, as it is the lentil husk extract provides the anti-inflammatory activity. Indeed, of the proanthocyanidins in the extract, it appears that prodelphinidin is most preferred.

Thus, there would have been no reason to add procyanidin from green tea leaves, or even from the lentil husk extract, to the composition of FOSTER for the purpose of treating inflammation.

III. There is no suggestion to optimize the amounts.

Neither CHARTERS nor RONZIO discloses an effective amount of either procyanidin, from lentil husk extract or green tea leaves, or N-acetyl glucosamine to treat inflammation.

Accordingly, one of ordinary skill in the art would have had no guidance to even approach the claimed ratio or amounts as recited in claims 3 and 4, respectively.

A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977).

IV. There is no recognition of a synergistic effect

The declaration filed July 13, 2007 demonstrated that the compounds have a synergistic effect when administered in combination for treating patients suffering from osteoarthritis of the knee. However, as applicant previously noted Boswellia extract "senolee" of the declaration was a typographical error, and that Boswellia extract serrata was actually evaluated. Accordingly, a corrected declaration is included in the appendix of the present amendment.

In order to prove that the results in the declaration demonstrate a synergistic effect, the pain data and the stiffness data from the declaration were analyzed according to the Bürgi formula. The Bürgi formula is a universally accepted formula in pharmacology (See Acta Pharmacol Sin 2004 Feb; 25(2): 146-147, included in the appendix of this Brief and the response filed

February 5, 2008). The results of the Bürgi formula analysis are discussed below:

q=observed value/expected value (the Bürgi formula) with a tolerance of ±0.15

where:
q=1 represents simple addition (i.e. additive effect)
q>1 represents synergism or potentiation
q<1 represents antagonism.

The expected value is the sum of the individual effects exerted by each compound, e.g., as administered to patient Groups 2-6. The individual effects are calculated as the difference between Day 0 and Day 14 values in Tables 1 and 2 below:

TABLE 1: Expected Value for Pain

Group	Effect
2	43.6 - 37.3= 6.3
3	43.7 - 37.3 = 4.6
4	43.5 - 41.1 = 2.4
5	45.1 - 42.8 = 2.3
6	44.9 - 44.5 = 0.4
Expected value for Pain	6.3 + 4.6 + 2.4 + 2.3 + 0.4 = **15**

TABLE 2: Expected Value for Stiffness

Group	Effect
2	42.4 - 44.1= -1.7
3	41.9 - 35.3 = 6.7
4	40.3 - 39.1 = 1.2
5	41.2 - 40.8 = 0.4
6	42.7 - 42.5 = 0.2
Expected value for Stiffness	-1.7 + 6.7 + 5.8 + 1.2 + 0.4 + 0.2 = **12.6**

The observed value is the effect of the combination of compounds, e.g., as administered to patient Group 7, which is calculated as the difference between the values from Day 0 and Day 14 in Tables 3 and 4:

TABLE 3: Observed Value for Pain (Group 7)
43.8 - 25.3 = **18.5**

TABLE 4: Observed Value for Stiffness (Group 7)
42.8 - 23.2 = **19.6**

Thus, parameter "q" based on Tables 1-4 above is:

q for Pain	**q for Stiffness**
18.5/15 = **1.23**	19.6/12.6 = **1.55**

As q is greater than 1, the compounds administered separately for Groups 2-6, i.e., Salix rubra extract, Boswellia serrata exact, Green tea extract, N-acetyl, glucosamine and Glucuronolactone, behave synergistically when administered together for Group 7, e.g., the claimed invention.

The standard deviation further suggests that the compounds exert a synergist effect. The difference in values between Day 0 and Day 14 in Groups 4, 5, and 6 are not statistically significant. That is, each single active compound fails to exert a significant effect on both pain and stiffness in the Day 0 to Day 14 period. The values for Group 7, however, are statistically significant for the same period.

Thus, the increased effect observed for Group 7 is attributed to the synergism of the five active compounds.

V. The combination fails to teach the claimed invention.

For the purpose of treating inflammation, at best, the combination may suggest a composition of saligenin, Boswellia serrata extract, a lentil husk extract, Japanese knotweed, Devil's claw, grapeskin and syzygium.

Therefore, for at least the five reasons discussed above, the proposed combination fails to render obvious claims 1-4, and withdrawal of the rejection is respectfully requested.

Claims 1-5, 7 and 8 were rejected under 35 USC §103(a) as being unpatentable over FOSTER, TANEJA, RONZIO, CHARTERS, SATO, as applied to claims 1-4, further in view of CHILTON U.S. 6,107,334 ("CHILTON"). This rejection is respectfully traversed for the reasons that follow.

FOSTER, TANEJA, RONZIO, CHARTERS and SATO were offered for the reasons discussed above.

CHILTON was offered for teaching dietary supplements for ameliorating inflammatory disorders. However, regardless of the ability of CHILTON to teach that for which it was offered, CHILTON does not remedy the shortcomings of FOSTER, TANEJA, RONZIO, CHARTERS and SATO for reference purposes.

Therefore, this combination fails to render obvious claims 1-5, 7 and 8, and withdrawal of the rejection is respectfully requested.

Conclusion

In view of the amendment to the claims and the foregoing remarks, this application is in condition for allowance at the time of the next Official Action. Allowance and passage to issue on that basis is respectfully requested.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our credit card which is being paid online simultaneously herewith for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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Appendix:

The Appendix includes the following item:

- Declaration Under Rule 132